

Meeting Summary

Human Genome Research in an Interdependent World

2 to 4 June 1991
Bethesda, Maryland, USA

From 2 to 4 June, 72 participants from 15 countries met in Bethesda, MD, to discuss international aspects of the social and ethical issues related to human genome research. The meeting was sponsored by the National Institute of Health's National Center for Human Genome Research through a grant to the University of Wisconsin. The Wisconsin Biotechnology Center, the USSR Academy of Sciences, and Japan's Science and Technology Agency provided additional support. The purpose of the meeting was to identify those issues that required attention at the international level. Forty-three speakers addressed a broad range of issues organized into ten general groupings in a very full agenda. Several topics were agreed to be appropriate for international activity, while others were deemed more appropriately dealt with at the national level or matters of science policy not specific to genome research. The issues identified as needing an international response proved to be too complex to be dealt with at a single international meeting many of whose participants were unfamiliar to one another, and before facts were gathered, international activity systematically surveyed, and policy options analyzed.

Conclusions from the meeting were tentative, and participants considered the meeting only a starting point for further analysis. The conferees did agree, however, on a structure to develop credible proposals to address the irreducibly international issues.

Participants agreed on a framework in which the international examination of these issues could take place. Programs to analyze the social, ethical, and legal aspects of genome research have been created in the Council of Europe, the Council for International Organizations of Medical Sciences (CIOMS), France, the

European Community (EC), the Human Genome Organization (HUGO), the International Association for Bioethics (IAB), Japan, the Netherlands, the USSR, the United Nations Educational, Scientific, and Cultural Organization (UNESCO), and the United States. The EC program on Ethical, Social, and Legal Aspects (ESLA) and the US program on Ethical, Legal, and Social Issues (ELSI), in particular, support significant research portfolios and will mount educational and outreach efforts. International efforts to grapple with ethical and social issues can thus build on a base of activity throughout the world, and should be integrated into existing national and intergovernmental efforts.

Issues considered important, but under active consideration elsewhere

Conflicts of Interest

A panel of speakers considered the potential for financial conflicts of interest in genome research, and the possible need for neutral scientific advice independent of commercial interests or government affiliations. Participants agreed the topic was germane to genome research, but not specific to it. Many areas of biomedical research, including drug trials, testing of medical devices, and industrially relevant science, are similarly subject to tensions between the roles of scientists as objective observers and parties with vested interests. Conflict of interest in biomedical research is undergoing intensive review in many sectors. Many conflicts can be avoided by the simple expedient of disclosing financial interests. Participants agreed that at a minimum, scientists should disclose their financial interests to their home institutions, but not all conflicts can be avoided by this measure alone. Most, although not all, issues arise in connection with applications of research rather than

basic undirected research, and will likely be less acute for mapping and sequencing efforts aimed at large chromosomal regions. Conflicts arising from applications will most logically be dealt with in the context of that specific application. Conflicts of interest are, moreover, not primarily international, although access to foreign experts might occasionally help resolve matters when financial interests of scientists in a country undermine their public credibility (as, for example, when the most respected investigators all have industrial affiliations).

The need for neutral advice and the potential for conflict of interest are not, however, specific to genome research, and standards applied in genome research should prevail elsewhere. Because it was not specific to genome research, and because most conflicts will be subject to national, rather than international, policies, this topic was considered best resolved by delegation to those organizations already engaged in formulating policies on conflict of interest.

Population Genetics

Collection of data on human population genetics is central to understanding the nature and extent of human genetic variation. Knowledge of such variation is necessary to understand human origins, including the timing and geography of historical migratory patterns. It is also central to interpreting forensic DNA tests used to identify individuals. Population genetic data can illuminate variations in DNA structure and function, mutation rates, and other detailed information of interest to molecular biologists studying individual genes.

HUGO recently designated an Advisory Committee on Human Genetic Variation to assess the feasibility of collecting, storing, analyzing DNA samples from representative populations throughout the world. The participants recognized the importance of the effort, and the immensely interesting data that will result. Several

issues could arise in such efforts, however, and meeting participants wished to request that the HUGO committee consider these when mapping out the strategy for collecting and storing DNA samples. First, the samples should be anonymous to the users. Samples should not include identifiers that will enable those using the data (other than the original investigator) to deduce from whom specific DNA samples were taken. The participants also expressed concern that the populations sampled be informed about the purposes of the research, be informed of its results, and be trained and equipped to participate directly in the research wherever possible in assembling such DNA sample collections. A member of the HUGO committee, Alberto Piazza, was present at the meeting and agreed to communicate these concerns.

Population genetics should also be instrumental in dispelling errant notions of "race." Speakers agreed that population genetic data will undermine attempts to overinterpret of minor genetic variations in order to reinforce preconceived, culturally grounded, stereotypes of "race." In large numbers of neutral genes studied to date, not subject to strong selection pressure, variation between individuals *within* populations exceeds that *between* different populations. Some traits are subject to selection pressure over shorter periods, so that variations are more readily apparent. Skin color, for example, correlates with climatic conditions, and hemoglobinopathies are associated with malaria prevalence. Measuring genes associated with such characters may well reveal population differences that correlate with the geographical origin of a person's recent ancestors. These are the rare cases, however. The vast majority of characters, such as strength, intelligence (of whatever variety), agility, and judgment, show intrapopulation variations greater than those between populations. Their inheritance is complex, and generally involves many genes. There can be no definitive classification of "races," but only arbitrary dividing

lines. Better public knowledge about population genetics could inoculate citizens against ideologically driven theories of race.

Issues appropriate for consideration by international task forces

Participants identified a group of issues too complex to address at the meeting, but with sufficient direct policy import to merit further work. Subsequent deliberations will require a larger group with more specialized expertise, the systematic collection of relevant data from around the world, and, in several cases, empirical data or more refined analysis possible only after further research. The participants recommended that these issues be tackled by task forces that will meet during the coming year and will report back to a parent steering committee in approximately one year. Depending on the amount and reliability of data and the complexity of the policy choices, some task forces might then dissolve, while others might require continued work.

Under-represented Nations

Two speakers, Chee Heng Leng and Vaclav Paces, noted the under-representation of developing nations and previously communist nations in genome research. A large cultural gap exists between genome researchers and the general population within their own countries. An even larger chasm separates genome researchers from third world populations. Some cultures may regard genetic analysis of diseases with considerable suspicion. Some may regard Western genetic research as an attempt to assert cultural dominance via science. Some may regard patent policies, for example, principally means to retain the economic benefits of new technologies for developed nations. Different cultures will regard resulting

data in widely disparate ways. Governments, particularly one-party or dictatorial ones, might misuse or misinterpret genetic data for political ends.

Another set of issues centers on integrating under-represented nations into the genome project. Scientists in under-represented nations must be trained so that they can participate in the project, and they will require computer and technical assistance. Developed nations may need to take special steps to convey information and technologies to nations unable to afford them. The transfer of inexpensive diagnostic technologies for diagnosis of high prevalence genetic diseases, or map and sequence data of special concern to those studying diseases of high local prevalence, might be delayed without direct policies to subsidize or otherwise encourage it.

Many participants noted that the meeting had insufficient representation from developing nations to formulate a complete list of issues. Indeed, the funding and composition of the meeting were evidence that the ethical and social issues in genome research are being identified and addressed only by those conducting the research, whereas the effects will be experienced by peoples in all nations. Participants also noted several times that analysis of the benefits and risks of applying technologies and information flowing out of the genome project should redound to the benefit of all, and that the usual channels of communications were often restricted to governments. Any future activities to analyze social impact in developing nations should take account of the fact that, in many cases, governments do not necessarily act in the best interests of those living within their jurisdiction. The recommendation was therefore to convene a task force whose specific function will be to elaborate issues of special concern to countries under-represented in genome research, and to develop recommendations about how to correct such problems.

Insurance and Employment

Genetic testing can provide substantial medical benefits for individuals, but test results will also have implications for employers and insurers. A host of issues regarding confidentiality and whether genetic information should be used to decide eligibility, scope, or cost of insurance are highly complex in any country. They are even more complex internationally. As barriers to international migration diminish, especially in Europe, as genetic tests become more plentiful and less costly, and as pressures to use tests mount, it would be useful to survey international practices and perhaps develop model statutes that could be used by many nations. This would be especially useful in the large number of nations that lack the policy analysis apparatus to think through the thicket of legal issues and technical considerations about actuarial practice and genetic testing methodology.

A task force must gather information relevant to the complex policy choices and conflicting interests, building on research efforts already begun under several national genome programs. The task force must also gather data on varying practices and policies around the world. In future discussions, it will be important to distinguish between policy options for health insurance, life insurance, disability insurance, employment, and other possible uses. The task force will investigate whether, and under what conditions, exceptions to applying general principles might be desirable regarding the collection and disclosure of genetic information. The possibility of developing ideas to prevent genetic discrimination through international law is tantalizing, and the task force might well encourage participation of the International Labor Organization and other international bodies in its deliberations.

Some issues will be primarily national in scope, and the task force may cull these out from more general issues of international concern. The coupling of health insurance to employment in the United States, for example, dramatically complicates access to health services, and thus how test results can reduce access. Issues related to life and disability insurance show many variations, although perhaps less dramatic, across national borders. The possible adverse impacts of various policy options, for example in reducing the number of jobs available by imposing overly restrictive guidelines, must also be considered.

Several principles should guide the use of genetic information that may have been obtained or will be collected by genetic testing. A subgroup of the speakers on this topic _ J. K. M. Gevers, N. A. Holtzman, and T. H. Murray _ formulated a tentative set of principles that a task force may refine. Individuals should only be treated after they receive a full disclosure and have given full and free consent. Individuals should have the choice of receiving the results of all tests, at their option. The information should include the implications of test results (whether positive, negative, or inconclusive) to the person tested and to relatives. Genetic information should be given to third parties only with the explicit consent of the person tested. Genetic information (including that derived from questions or from previous tests) should not be used to deny or constrict employment opportunities, to limit access to health care, or to deny a reasonable level of economic security for oneself or one's dependents. Genetic tests should be adopted only when their validity has been established and when a system for monitoring laboratory proficiency is in place. Other types of medical information should be accorded the same protection as described for genetic information.

Forensics

The use of DNA tests to identify individuals is increasingly used in legal proceedings. It is often used to link evidence from a crime _ most often rape and murder _ to its perpetrator, or to exonerate those wrongly accused. Forensic testing is also used to establish relatedness of individuals for immigration purposes, or to enforce child support statutes. Those practicing DNA forensics were encouraged to improve the population genetic databases used to interpret results, to develop better methods for DNA typing, and to establish standards for quality assurance and proficiency testing. DNA testing is a valuable tool for pursuing justice, but it does raise some ethical issues. Most of these are primarily subject to national, rather than international, in scope. A few, however, merit attention at the international level. If one nation requests genotype from another in a criminal investigation, for example, for what crimes should such data be donated? What are the assurances that civil liberties protected in the donor country will also be respected in the country requesting data? When there are differences of national practice regarding capital punishment (or other penalties regarded as morally acceptable in one culture but not another), should data pertinent to crimes bearing this punishment be exchanged?

The meeting also considered proposals to standardize DNA identification techniques across national boundaries. Practices in North America and Europe have already begun to diverge (using different restriction enzymes and probes). Such differences may hamper cooperative law enforcement work, could drive up costs by requiring retesting, and could potentially necessitate the retention of DNA samples rather than genotype data. Retention of DNA samples is both more costly, more technically demanding, and carries with it the temptation to use DNA samples for uses other than its originally intended purposes. Finally, the development of international standards might well improve the process of introducing DNA

evidence into domestic courts, and might reduce the difficulties of commencing DNA forensic testing in countries not yet using it.

Participants noted the trend to establish DNA collections for forensic purposes. Several questions arise in connection with such collections, and these may well become pertinent to international discussion as DNA forensic testing diffuses into more countries.

Should DNA or only genotype data be stored?

If DNA is retained, should there be time limit?

What are the protections on confidentiality of data?

Should there be constraints on uses other than for identification of criminals? If

DNA samples are stored, should they be used for any purposes other than those for which they were originally intended? Should they be used to find matches for bone marrow donors, for example?

On whom should genotypes be performed, or DNA samples taken? Only those convicted of rape or murder? Those convicted of violent crimes? Those convicted of felonies? Misdemeanors?

How should abuses of DNA testing techniques in countries with inadequate civil liberties guarantees be deterred? What curbs should there be on sharing data and techniques with internal security forces of these governments?

Issues referred to an international coordinating committee

The participants identified a group of issues that were not discussed at the workshop sufficiently to formulate specific tasks for further analysis. These topics will be considered by the coordinating committee which can form future task forces if need be.

Clinical uses

Treatment of early embryos, sperm cells, egg cells, or their precursors would lead to inherited changes in all or some fraction of an individual's progeny.

Whether or not such germ line gene therapy should proceed has been discussed by a variety of governments, religious groups, and nongovernment organizations. The

recommendations of these various groups vary. The German parliament proscribed germ line gene therapy, for example, while a multidisciplinary CIOMS workshop urged continued public discussion but no "premature foreclosure" on the issue of whether it might some day be desirable. Discussion at the workshop yielded no consensus. Participants also differed about whether gene mapping and sequencing were closely related to genome research, and should be considered in ethical discussions about such research, or whether such discussion was best conducted in a forum focused on gene therapy itself.

Genetic testing and screening will undoubtedly increase as more genetic conditions are mapped, and as diagnostic methods improve. Genetic services differ markedly across countries, and the ethical and social dimensions of how to approach such differences are not yet clear. One issue of particular concern is prenatal diagnosis. Different cultures will use genetic tests for different conditions, and the availability of abortion following prenatal diagnosis is quite different among nations. This set of issues merits further inquiry, but was not the subject of a session at the meeting.

Intellectual Property

Different nations have different criteria for granting patents, and this has a bearing on the direction of genome research, and also on how and when research results are made public. Many groups have studied international differences in patent law, and are working to narrow such differences. Some differences, however, are based at least in part on arguments about morality. The patenting of animals, for example, has occurred in the United States but not in Europe. Plant patent practices also vary, in part turning on different conceptualizations of how patent law

relates to living things. This was another rich topic area not explored deeply at the meeting.

Other functions of the coordinating committee

Several participants suggested specific additional functions that the coordinating committee might perform. A scholar or group of scholars might be commissioned to review immigration statutes from throughout the world with an eye to identifying provisions that retain vestiges of eugenic justification. The coordinating committee might develop a model statute or make specific recommendations on changes in existing laws. The committee might also monitor the activities of specific governments thought to be formulating or implementing overtly eugenic policies. Activities in Singapore (economic incentives to produce children among university graduates) and China (abortion of female fetuses following genetic typing) were raised as examples that might merit investigation.

Composition of the coordinating committee

Participants included representatives from these organizations, who concurred that the specifically international aspects of several issues were not being directly addressed, but could be accommodated by periodically convening a coordinating committee with the following representation:

- Council of Europe (1)

- Council of International Organizations of Medical Sciences (3: 1 with expertise in convening international meetings, 1 from the third world, and 1 from patient organizations)

- EC Working Group on Ethical, Social, and Legal Aspects of Genome Research (1)

- Human Genome Organization (2: 1 from Europe, 1 from North America)

- International Association of Bioethics (1)

- Japan (1)

- NIH-DOE Joint Working Group on Ethical, Legal, and Social Issues (1)

- UNESCO (1)

- USSR (1)

The participants recommended that the coordinating committee meet once in the next several months, along with representatives of potential funding groups, to map an initial approach to forming task forces and commissioning urgently needed research. The committee will meet periodically thereafter, perhaps annually, to assess progress, to adjust plans, and to implement recommendations of the task forces.